

Remarks

Claims 1, 3-8, and 10-21 are pending in the application. Claims 12-16 have been withdrawn from consideration. Claims 1, 3-8, 10, 11, and 17-21 stand rejected.

Claims 3, 18, and 19 have been canceled by the present Amendment.

Claims 1, 4, 6, 20, and 21 have been amended. Support for the Amendment to claims 1 and 6 can be found throughout the specification, for example, in paragraphs 39 and 54. Claims 4, 20, and 21 have been amended to correct the dependencies of those claims.

New claims 22-59 have been added. Support for new claims 22-24 and 37 can be found throughout the specification, for example, in paragraph 26. Support for new claims 25, 35, and 59 can be found throughout the specification, for example, in Example 19. Support for new claim 26 can be found throughout the specification, for example, in paragraphs 24, 36, and 40. Support for new claims 27-29 and 31-33 can be found throughout the specification, for example, in paragraphs 33, 37, and 39. Support for new claims 30 and 34 can be found throughout the specification, for example, in paragraph 31. Support for new claim 36 can be found throughout the specification, for example, in paragraphs 26, 33, 45, and 81. Support for new claim 38 can be found throughout the specification, for example, in paragraph 53. Support for new claim 39 can be found throughout the specification, for example, in Examples 1 and 2. Support for new claims 40 and 43 can be found throughout the specification, for example, in paragraph 54 and in Examples 3, 9, and 10. Support for new claim 41 can be found throughout the specification, for example, in Example 15. Support for new claim 42 can be found throughout the specification, for example, in paragraph 48. Support for new claims 44-46 and 52-54 can be found throughout the specification, for example, in paragraphs 37-39 and 53. Support for new claims 47 and 55 can be found throughout the specification, for example, in paragraph 33 and Example 16. Support for new claims 48 and 56 can be found throughout the specification, for example, in paragraph 36 and Examples 16 and 17. Support for new claims 49, 50, 57, and 58 can be found throughout the specification and in original claim 3. Support for new claim 51 can be found throughout the specification, for example, in paragraph 48 and Example 15.

No new matter has been added by the present Amendment. Applicant specifically reserves the right to pursue the subject matter of the canceled or amended claims in a related application. The present Amendment is introduced for the sole purpose of furthering prosecution. Applicant respectfully requests reexamination and reconsideration of the case in

light of the present Amendments and the following remarks. Each of the rejections levied in the Office Action is addressed individually below.

Interview

Applicant thanks the Examiner for a telephone interview that took place on April 9, 2009, at which the present rejections were discussed. The Examiner and Applicant discussed claim Amendments that will obviate the rejections under 35 U.S.C. § 102 and 103. Among other things, the Examiner indicated that amending the claims to specify that the PP2A methylation assay contains PP2A, PP2A methylase enzyme, *and* PP2A demethylase enzyme might suffice to overcome the §§ 102 and 103 rejections, as he agreed that such disclosure is not in the cited references.

Rejection under 35 U.S.C. § 102(b) for alleged lack of novelty

Claims 1, 3, 6-8, and 17-21 stand rejected under 35 U.S.C. § 102(b) on the ground that they are anticipated by Lee *et al.* (1996, *Proc. Natl. Acad. Sci., USA*, 93:6043-47). The Examiner states that Lee (1) teaches methods for identifying a compound that is responsible for demethylation of PP2A, and (2) shows inhibition of a demethylation reaction of PP2A by a compound (*i.e.*, okadaic acid) identified by those methods. Applicant respectfully disagrees.

As an initial matter, Applicant submits that the Examiner's reading of the okadaic acid experiment in Lee is not quite accurate. Okadaic acid is not a compound identified by any of the methods described in Lee. Okadaic acid was already known to be an inhibitor of PP2A *methylation*, and Lee shows that okadaic acid is also an inhibitor of PP2A *demethylation* (page 6046, first column, first full paragraph). Thus, okadaic acid inhibits *both* PP2A methylation *and* demethylation. Lee also notes that okadaic acid is a specific, *direct* inhibitor of PP2A phosphatase activity (page 6046, first column, first full paragraph of Lee; and Example 19 of the present specification). Okadaic acid's effect on PP2A phosphatase activity is not dependent on affecting PP2A methylation status. Indeed, okadaic acid affects PP2A phosphatase activity *directly*. Thus, okadaic acid has three *independent* effects on PP2A: (1) inhibits PP2A methylation, (2) inhibits PP2A demethylation, and (3) inhibits phosphatase activity of PP2A.

With that background in mind, Applicant respectfully submits that Lee does not anticipate the present claims. Although Applicant submits that the *original* claims were not

anticipated by Lee, Applicant has made claim amendments that even more clearly distinguish the claims from Lee, *solely* in order to further prosecution. The present claims involve a PP2A assay containing PP2A, a PP2A methylase enzyme, *and* a PP2A demethylase enzyme. Lee does not describe an assay which includes both the methylase and demethylase.

Applicant notes that various of the present claims include additional features that clearly distinguish PP2A modulators of the present claims from okadaic acid. For example, new claim E specifies that the test agent or composition interferes with PP2A subunit assembly. In contrast, okadaic acid does not interfere with PP2A subunit assembly. In addition, new claim 25 specifies that the test agent or composition affects phosphatase activity of PP2A through its effects on PP2A methylation. As already noted, okadaic acid is known to *directly* affect PP2A phosphatase activity, so it is clear that okadaic acid's effects on PP2A activity are not through an effect on PP2A methylation. Indeed, Example 19 of the present specification describes synthesis of a library of candidate test agents which affect PP2A methylation, but do not have direct effects on PP2a phosphatase activity. Thus, when the application was filed, the present inventors clearly did not intend for the methods recited in the present claims to identify okadaic acid as a PP2A modulator, but intended for the claimed methods to identify agents that affect phosphatase activity of PP2A through their effects on PP2A methylation.

In order to anticipate, a reference must teach *every element* of the claimed invention. Lee does not teach all of the steps recited in the pending claims. Nor does Lee (or the art relating to okadaic acid) teach compounds identified by the methods recited in the present claims. Applicant, therefore, respectfully submits that Lee does not anticipate the present claims and respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 103(a) as allegedly being obvious

Claims 4, 5, 10, and 11 stand rejected under 35 U.S.C. § 103(a) on the ground that they are unpatentable over Lee *et al.* in view of Roder *et al.* (U.S. Patent 6,541,468). The Examiner states that the claims differ from Lee in that they specify that the protein activity is phosphorylation of tau, which is hyperphosphorylated, and the compound modulates methylation of PP2A, thereby decreasing tau hyperphosphorylation. The Examiner states that Roder describes that it is desirable to have a pharmaceutical means of interfering with tau hyperphosphorylation. The Examiner, therefore, states that it would have been obvious to one of

ordinary skill in the art to modulate PP2A activity by demethylating the enzyme, as taught by Lee, in order to reduce hyperphosphorylation of tau, because Roder teaches the relationship between PP2A activity and pathological tau hyperphosphorylation. Applicant respectfully disagrees.

The deficiencies of Lee are described in detail above. In particular, Lee does not describe every element of the present claims. Roder (which was cited only for its general disclosure relating to tau hyperphosphorylation) does not remedy the deficiencies of Lee. Applicant, therefore, respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite

Claims 1, 3-8, 10, 11, and 17-21 stand rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they are indefinite. In particular, the Examiner states that in claim 1 and all occurrences, the preamble of the claim is directed to “identifying agents,” but the claim lacks any such step. Applicant respectfully disagrees. Without agreeing with the Examiner, however, and solely in order to further prosecution, Applicant has amended claims 1 and 6 to include a step of “identifying” agents or compositions. Applicant has canceled claims 3 and 19. Applicant, therefore, respectfully requests that the rejection be removed.

The Examiner states that claims 17 and 18 lack antecedent basis for recitation of “the PP2A methylation assay.” Applicant respectfully disagrees. Applicant has canceled claim 18, and respectfully submits that the rejection as it applies to claim 18 is, therefore, moot. Claim 17 depends from claim 1 or 3, both of which explicitly recite “a PP2A methylation assay” (line 5 of claim 1, and line 6 of claim 3). Applicant, therefore, respectfully submits that recitation of “the PP2A methylation assay” in claim 17 has sufficient antecedent basis. Applicant respectfully requests that the Examiner withdraw the rejection and correct the record.

The Examiner states that the preamble of claim 19 is directed to compositions, but the steps are directed to “candidate test agents” and “the composition.” Applicant has canceled claim 19 and, therefore, respectfully submits that the rejection is rendered moot by the present Amendment.

Title of the Invention

The Examiner further states that the title of the invention is not descriptive and that a new title is required that is clearly indicative of the invention to which the claims are directed. Applicant respectfully disagrees and submits that the title is descriptive. Solely in order to further prosecution, however, Applicant respectfully requests that the Examiner suggest a title that would be acceptable.

Conclusion

For all of the reasons set forth above, each of the rejections in this case should be removed and the application should proceed to allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5175.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

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